Which Technique for Plaque Evaluation: Stable vs Vulnerable IVUS or HD-IVUS and VH-IVUS

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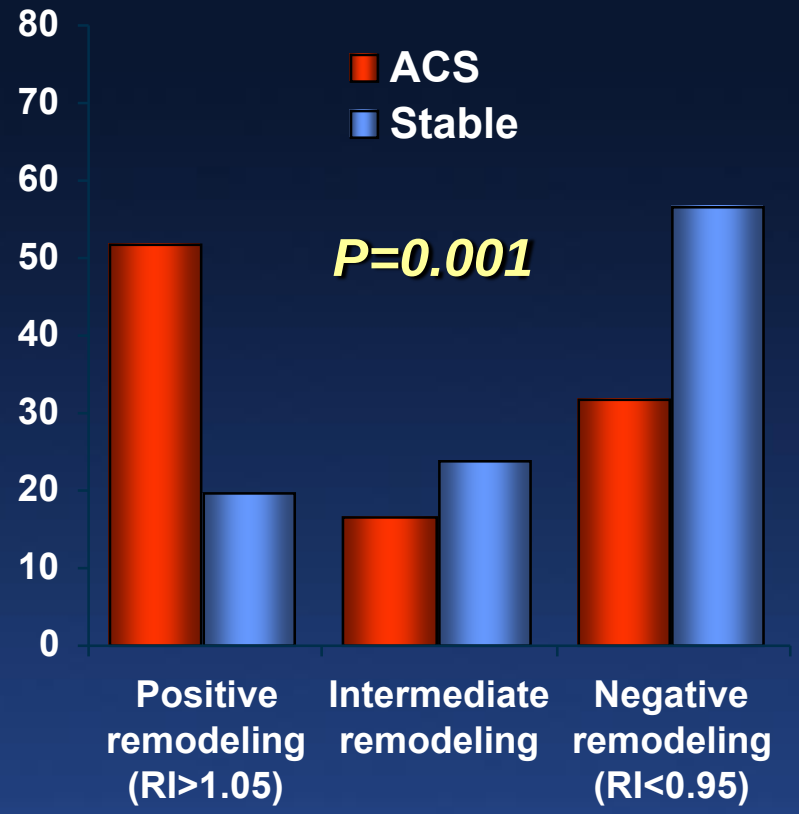
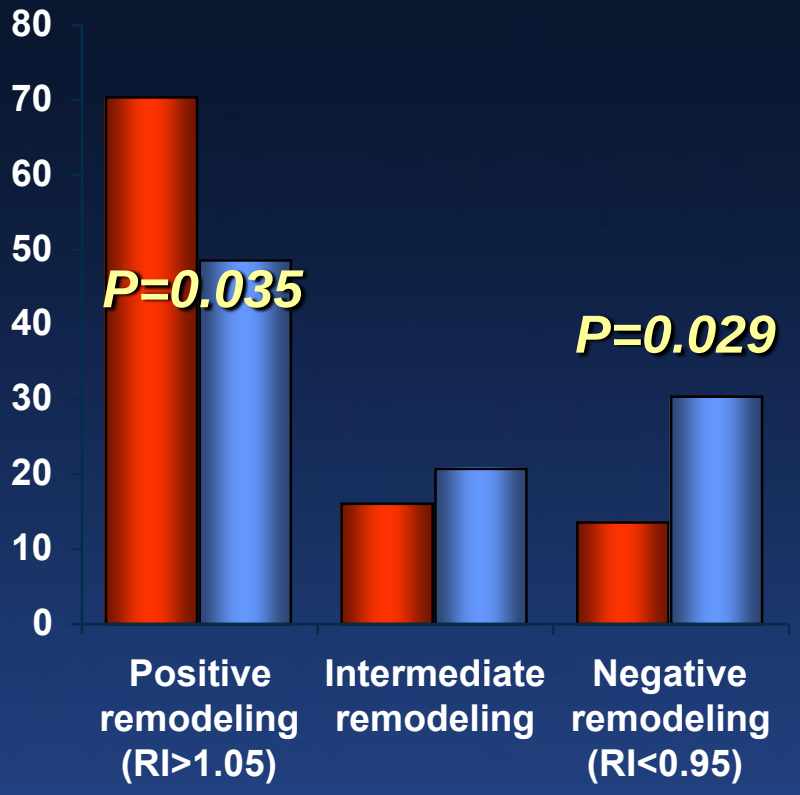
Clinical syndromes	Grayscale IVUS	VH-IVUS
Acute coronary syndromes	Positive remodeling	Necrotic core
Distal embolization during PCI	Echolucent plaque	VH-TCFA
	Attenuated plaque	
	Spotty calcification	
	Ruptured plaque	
	Calcified nodule	

More than a dozen studies have reported the association between positive remodeling and unstable lesion morphology



(Schoenhagen et al. Circulation 2000;101:598-603)



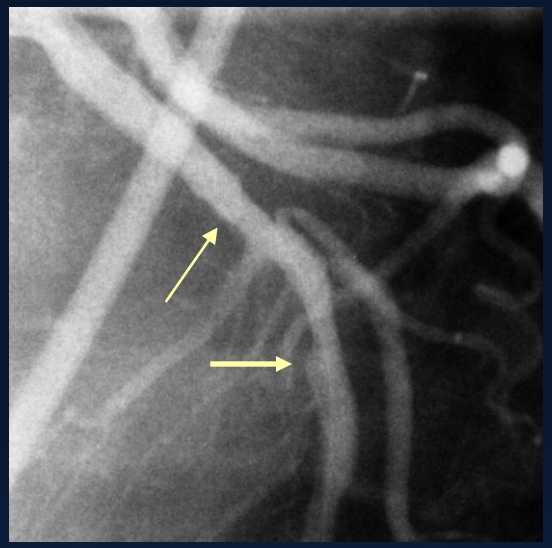
(Prati et al. Circulation 2003;107:2320-5)

Morphology of vulnerable coronary plaque: insights from follow-up of patients examined by IVUS before an acute coronary syndrome

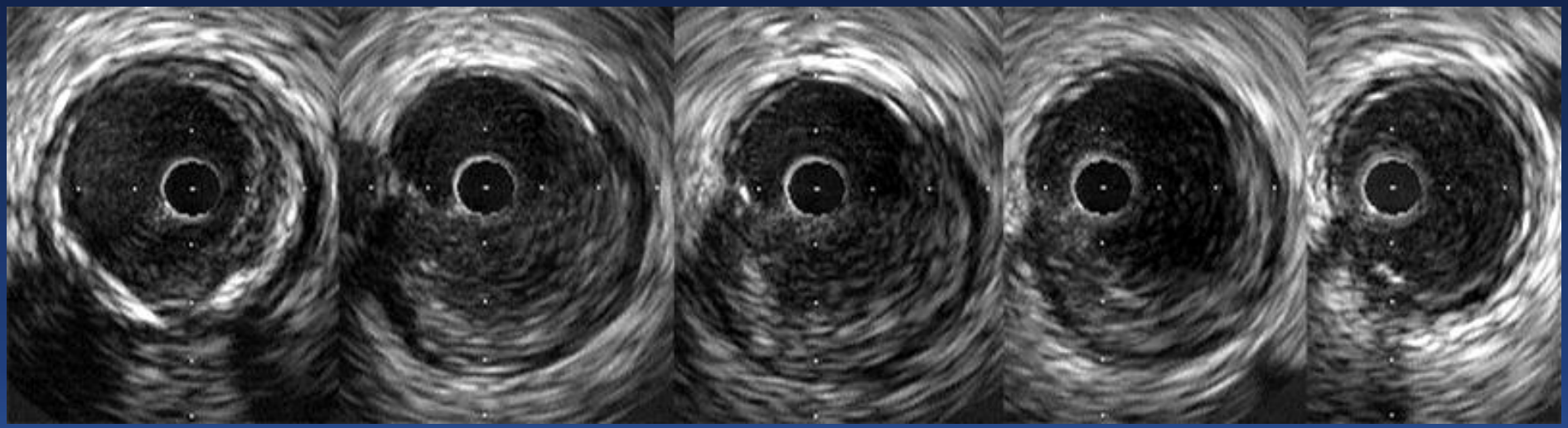
- 114 coronary sites from 106 patients
- 16 pts had an acute event 1-24 months (21.8±6.4months) post index IVUS
- 12 pts had the event 4.0±3.4 months (range 1 to 8 months) at the same sites where preexisting atherosclerotic disease had been demonstrated by IVUS

	Sites related to acute events	Sites not related to acute events	p
Plaque burden	67±9%	57±12%	<0.05
Shallow echolucent zones	8/12	4/90	<0.05

(Yamagishi et al. J Am Coll Cardiol 2000;35:106-11)



Proximal 0 → 3mm → 12mm



EEM CSA = 21.0mm²

EEM CSA = 23.5mm²

EEM CSA = 13.7mm²

Spotty Calcification in ACS/MI

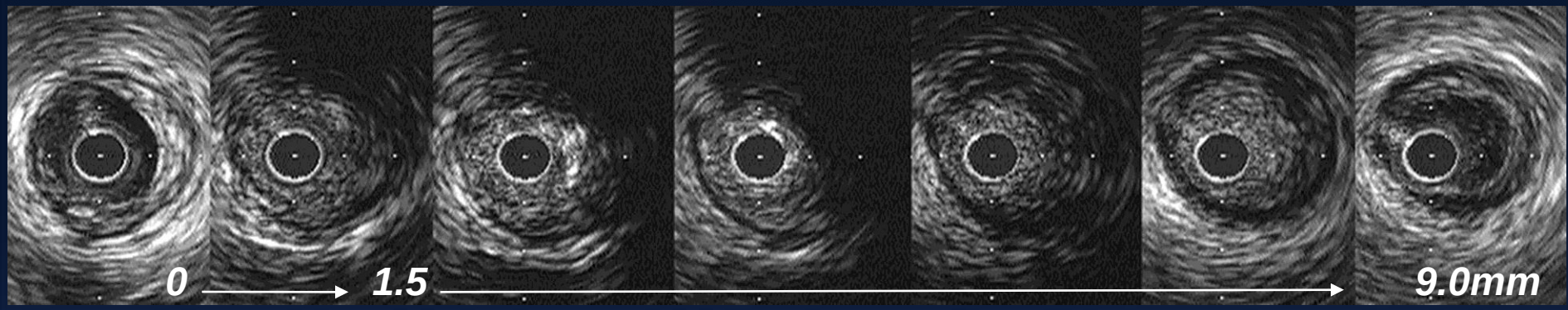
	MI (n=61)	ACS (n=70)	Stable Angina(n=47)
No calcium	26%	41%	21%
Spotty calcium	51%	40%	30%
Intermediate calcium	15%	16%	11%
Extensive calcium	8%	3%	38%

Overall, p<0.0001

- ***Spotty calcification = only small calcium deposits <90°***
- ***Intermediate calcification = 90-180° in at least 1cross-section***
- ***Extensive calcificaiton = >180° in at least 1 cross-section***

Ehara et al. Circulation 2004;110:3424-9

Attenuated Plaque



- *Attenuated plaques were seen in 39.6-78.0% of STEMI, 17.6% of NSTEMI, and 0% of stable angina.*
- *Attenuate plaques were associated with more fibroatheromas and a larger necrotic core (on VH-IVUS).*
- *In ACS or MI pts with attenuated plaques (1) the level of CRP was higher, (2) angiographic thrombus and initial coronary flow <TIMI 2 were more common, and (3) no-reflow or flow deterioration post-PCI was also more common.*
- *In STEMI patients with attenuated plaques, the amount, not the presence, of attenuated plaque predicted no-reflow or MRI-derived microvascular obstruction post stent implantation*
- *Attenuated plaque was associated with the presence of TCFA, ruptured plaques, thrombus, and greater lipid content*
- *Attenuated plaques contained the highest NIRS probability of lipid core, and by VH-IVUS, 93.5% of attenuated plaques contained confluent necrotic core and were classified as fibroatheromas*

(Lee et al. JACC Cardiovasc Interv. 2009;2:65-72)
(Wu et al, Am J Cardiol 2010;105:48-53)
(Okura et al, Circ J 2007;71:648-53)
(Wu et al. JACC Cardiovasc Interv 2011;4:495-502)
(Lee et al JACC Cardiovasc Interv. 2011;4:483-91)
(Kubo et al. Cardiol Res Pract. 2011;687515)
(Pu et al. Eur Heart J 2012;33:372-83)
(Shiono et al, JACC Cardiovasc Interv 2013;6:847-53)

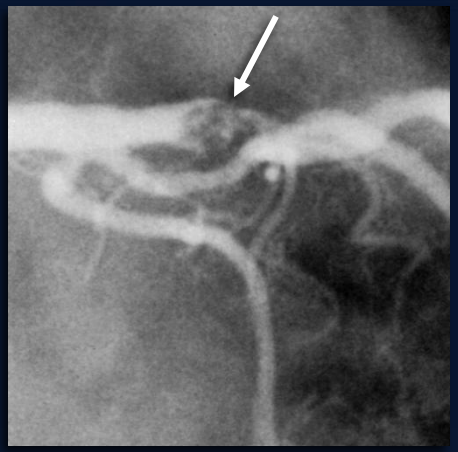
Grayscale IVUS predictors of large (>20%) histopatholgic lipidic/necrotic core (n=2294 coronary artery segments)

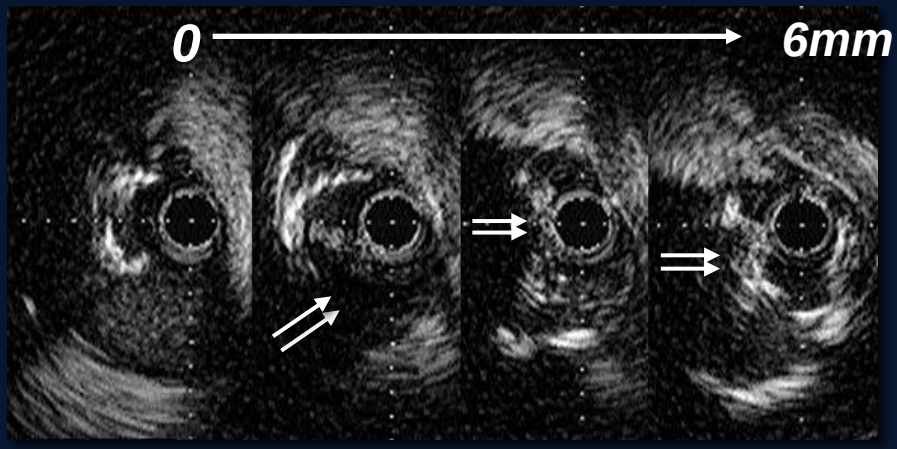
	Sensitivity	Specificity	PPV	NPV
Echolucent plaque	20.5%	90.4%	77.3%	49.8%
Spotty calcification	69.4%	71.7%	62.4%	77.5%
Echo-attenuated plaque	56.2%	94.7%	91.4%	54.6%

96.3% of superficial echo-attenuated plaque, 82.8% of superficial echolucent plaque, and 72.6% of superficial spotty calcification indicated a FA with a large lipid/necrotic core

Culprit plaque ruptures in ACS/AMI studied with 3 vessel imaging

		# of pts	Culprit plaque ruptures	Secondary plaque ruptures
Riouful. Circulation 2002;106:804-8	IVUS	24	38%	79%
Hong. Circulation 2004;110:928-33	IVUS	122	66%	17%
Tanaka. J Am Coll Cardiol 2005;45:1594-9	IVUS	45	47%	24%
Fujii. J Am Coll Cardiol 2008;52:787-92	OCT	35	46%	31%
Tanaka. Am J Cardiol 2008;102:975-9	OCT	43	65%	12%
Kubo. Am J Cardiol 2012;105:318-22	OCT	26	77%	12%
Kukunaga. Eurointervention 2012;8:955-61	OCT	70	46%	31%
Xie. JACC Cardiovasc Imaging, in press	IVUS (20MHz)	660	N/A	14%
Average	IVUS		58%	17%
	OCT		55%	





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American Heart Journal

Intravascular ultrasound identification of calcified intraluminal lesions misdiagnosed as thrombi by coronary angiography

Gaston R. Duissaillant, MD, Gary S. Mintz, MD, Augusto D. Pichard, MD, Kenneth M. Kent, MD, PhD, Lowell F. Satler, MD, Jeffrey J. Popma, MD, Jennifer Griffin, BS, and Martin B. Leon, MD
Washington, D.C.

Accurate identification of coronary atherosclerotic plaque composition is important for optimum patient management and transcatheter therapy. In particular, the presence of thrombus typically leads to protracted hospitalization, intravenous or intracoronary thrombolysis, prolonged systemic anticoagulation, and the use of transcatheter devices designed to remove thrombi. Furthermore, thrombi may be implicated in poor outcome after transcatheter therapy. Intraluminal filling defects are believed to be the most specific angiographic markers of thrombus. We report three patients with intracoronary filling defects initially diagnosed as thrombus; however, intravascular ultrasound (IVUS) imaging showed that these filling defects represented calcified nodules.

IVUS studies were performed with one of two commercially available systems. The first (Cardiovascular Imaging Systems Inc./InterTherapy Inc., Sunnyvale, Calif.) incorporated a single element 25-MHz transducer and an angled mirror mounted on the tip of a flexible shaft that was rotated at 1800 rpm within a 3.9F short monorail polyethylene imaging sheath to form planar cross-sectional images in real time. The second (Cardiovascular Imaging Systems) incorporated a single element 30-MHz beveled transducer within either a 2.9F long monorail imaging catheter having a common distal lumen design (the distal lumen alternatively accommodates the imaging core or the guide wire, but not both) or within a 3.2F short monorail imaging catheter. With both systems the imaging catheter was advanced 5 to 10 mm beyond the target lesion and the transducer was withdrawn automatically at 0.5 mm/sec within the imaging sheath to perform the imaging sequence. IVUS studies were recorded on ½-inch high resolution s-VHS tape for offline analysis.

Patient 1. A 78-year-old white man with a history of pneumoconiosis, gastrectomy for stomach cancer, congestive heart failure from dilated cardiomyopathy, and coronary artery disease was seen for progressive angina. A coronary angiogram showed a 95% ostial right coronary artery lesion with a round filling defect highly suggestive of thrombus. He was treated with heparin and sent home taking coumadin to dissolve the thrombus. However, he returned with worsening angina; coronary angiography still showed a large filling defect almost completely occluding the right coronary artery (Fig. 1). He was initially treated with an intracoronary urokinase infusion of 250,000 U followed by the use of a 2.2-mm transluminal extraction atherectomy cutter (Interventional Technologies, Inc., San Diego, Calif.) and 3.5-mm adjunct balloon

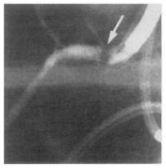


Fig. 1. Proximal right coronary artery filling defect *(arrow)* was initially thought to represent intracoronary thrombus. Patient was treated with prolonged system anticoagulation, intracoronary thrombolysis, and extraction atherectomy. IVUS imaging showed that filling defect was, in fact, calcified lesion protruding into lumen.

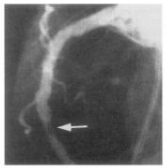


Fig. 2. Mid-right coronary artery filling defect *(arrow)* was initially thought to represent intracoronary thrombus. Patient was also treated with prolonged systemic anticoagulation. IVUS imaging showed that filling defect was, in fact, calcified lesion protruding into the lumen. Because of limited device availability, patient was referred for bypass graft surgery.

From the Intravascular Ultrasound Imaging and Cardiac Catheterization Laboratories, Washington Hospital Center.
Supported in part by the Cardiology Research Foundation, Washington, D. C.

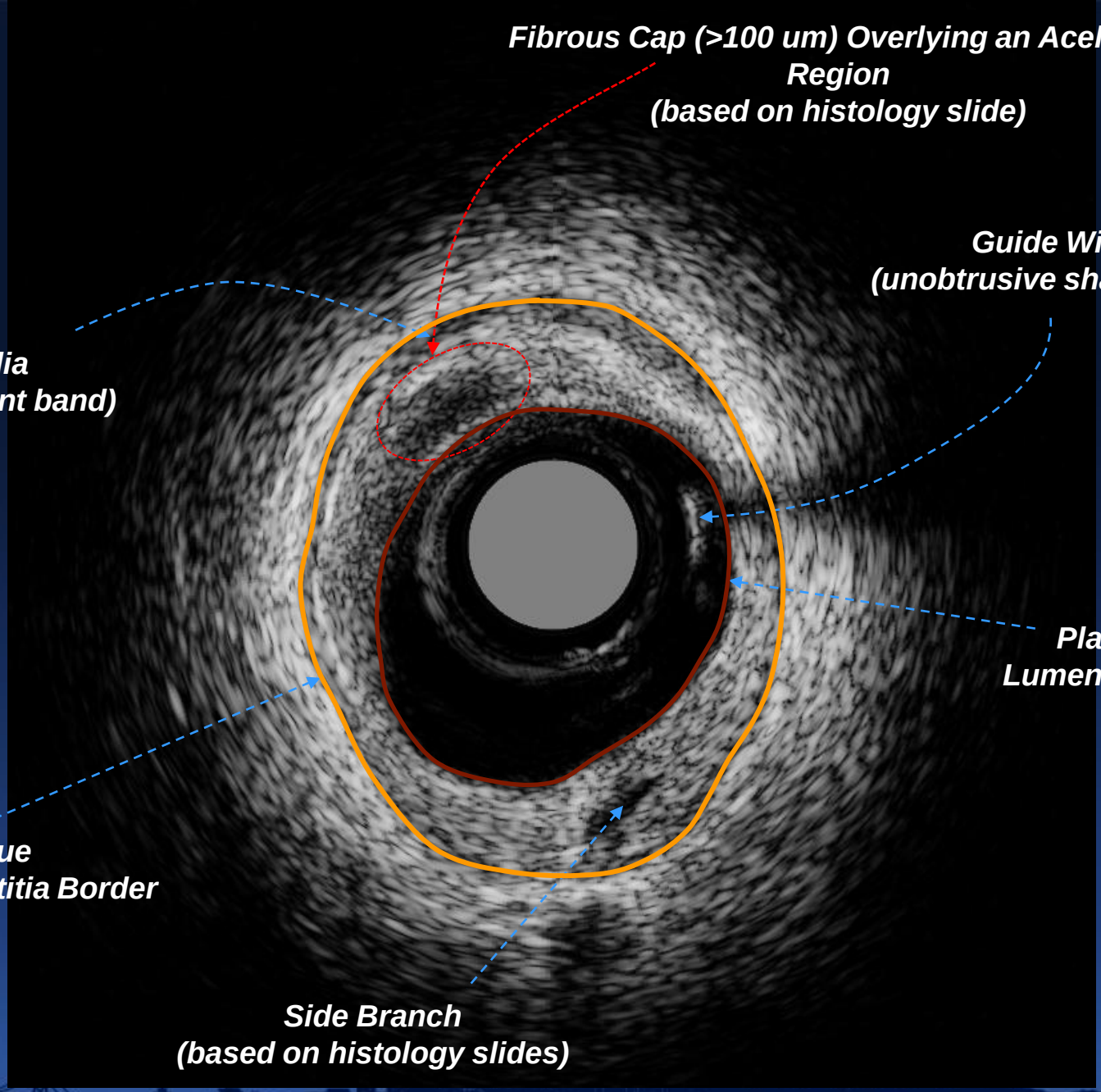
Reprint requests: Martin B. Leon, MD, Washington Cardiology Center, 110 Irving St., NW, 4B-1, Washington, DC 20010.

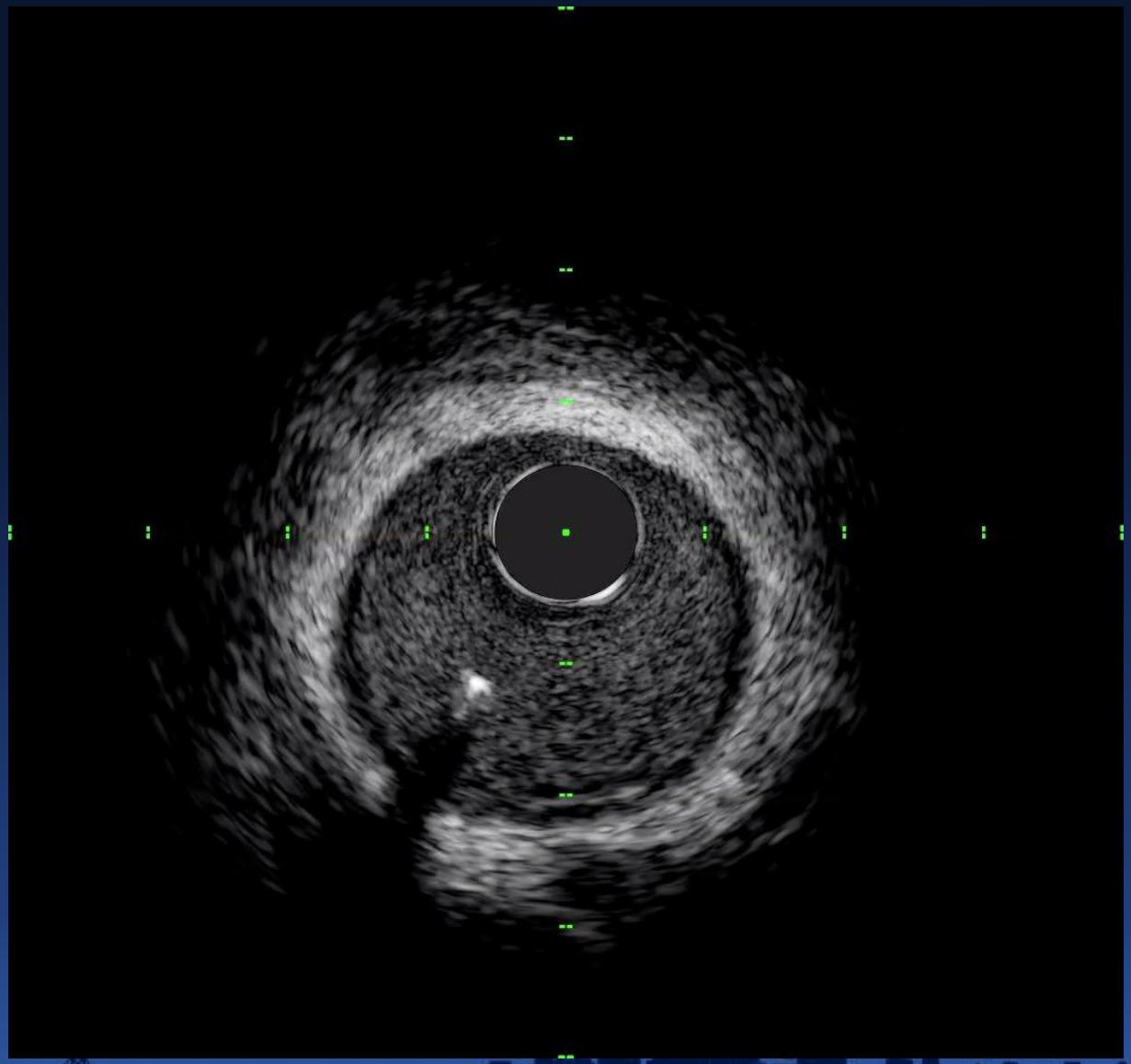
Am Heart J 1996;132:687-9.

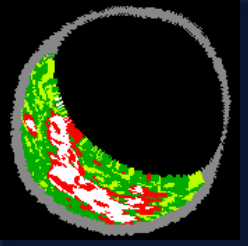
0002-8703/96/$5.00 + 0 4/4/71890

"We present three patients with classical angiographic features of intracoronary thrombus in whom IVUS imaging showed that the filling defects were not thrombi, but calcified (presumably atherosclerotic) masses."

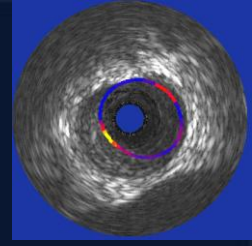
Dussaillant et al. Am Heart J 1996;132:687-9


Fibrous Cap (>100 um) Overlying an Acellular Region
(based on histology slide)
Guide Wire
(unobtrusive shadowing)
Media
(echolucent band)
Plaque
Lumen Border
Plaque
Media-Adventitia Border
Side Branch
(based on histology slides)





The PROSPECT Trial



700 pts with ACS UA (with ECG Δs) or NSTEMI or STEMI >24º undergoing 1 or 2-vessel PCI followed by 3-vessel imaging

QCA of entire coronary tree

IVUS

Virtual Histology

Proximal 6-8 cm of each coronary artery

Medications
Aspirin
Plavix ≥1yr
Statins

F/U: Until there were 100 VP events

Repeat imaging in patients with events

PROSPECT: Multivariable Correlates of Non Culprit Lesion Related Events

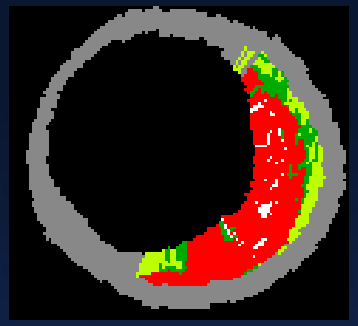
Independent predictors of lesion level events by Cox Proportional Hazards regression

Variable	HR [95% CI)	p
PB_{MLA} ≥70%	5.03 [2.51, 10.11]	<0.0001
VH-TCFA	3.35 [1.77, 6.36]	0.0002
MLA ≤4.0 mm^2	3.21 [1.61, 6.42]	0.001

Variables entered into the model: minimal luminal area (MLA) ≤4.0 mm^2; plaque burden at the MLA (PB_{MLA}) ≥70%; external elastic membrane at the MLA (EEM_{MLA}) <median (14.1 mm^2); lesion length ≥median (11.2 mm); distance from ostium to MLA ≥median (30.4 mm); remodeling index ≥median (0.94); VH-TCFA.

Stone et al. N Engl J Med 2011;361:226-35

PROSPECT: Predictors of Non Culprit Lesion Events



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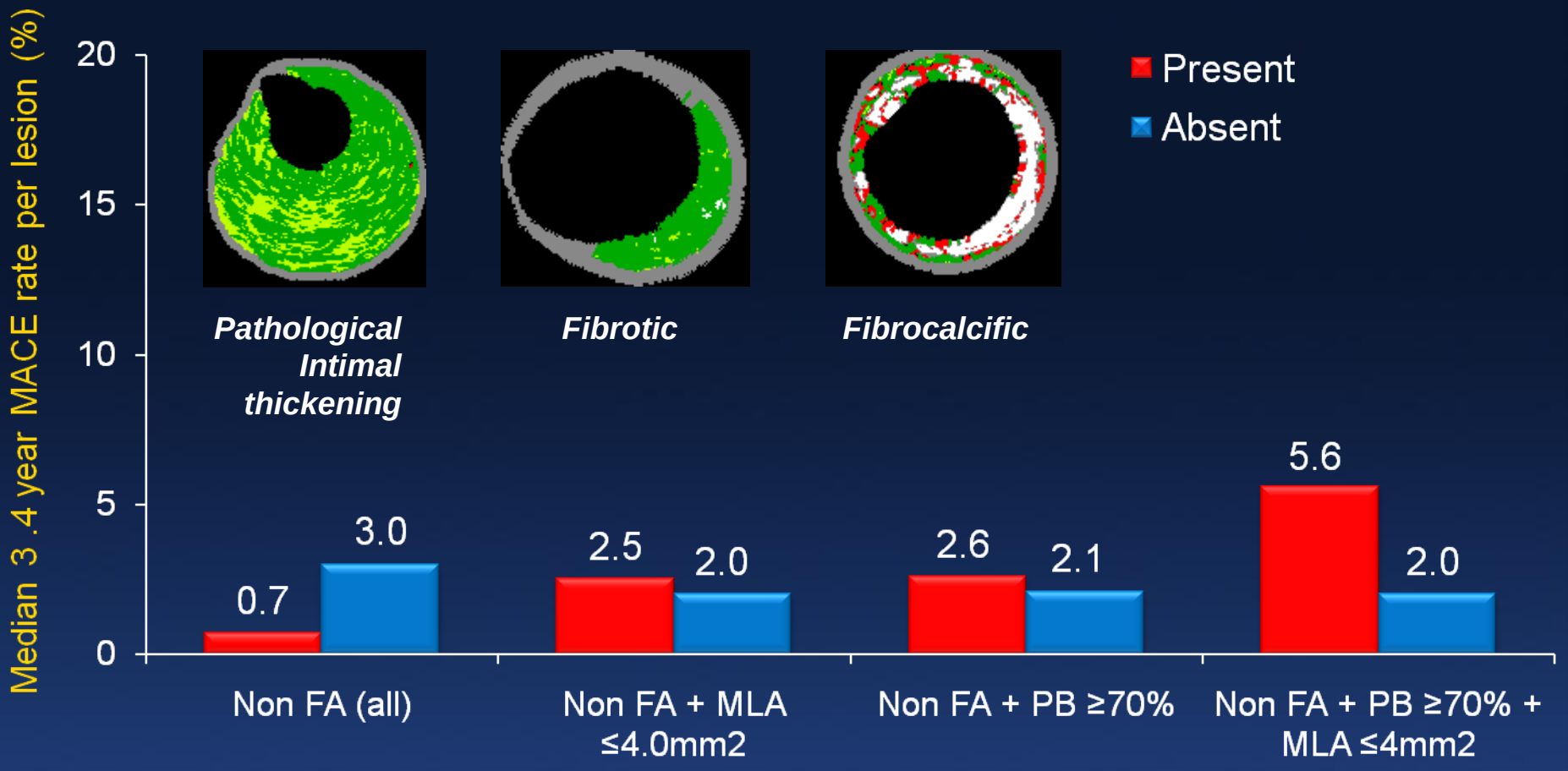
Stone et al. N Engl J Med 2011;361:226-35

Non Fibroatheromas and Non Culprit Lesion Events



Lesion HR	0.22 [0.10, 0.49]	1.49 [0.44, 3.39]	1.25 [0.17, 9.01]	2.60 [0.36, 18.84]
P-value	0.0002	0.70	0.83	0.34
Prevalence	67.9%	19.7%	5.6%	2.7%

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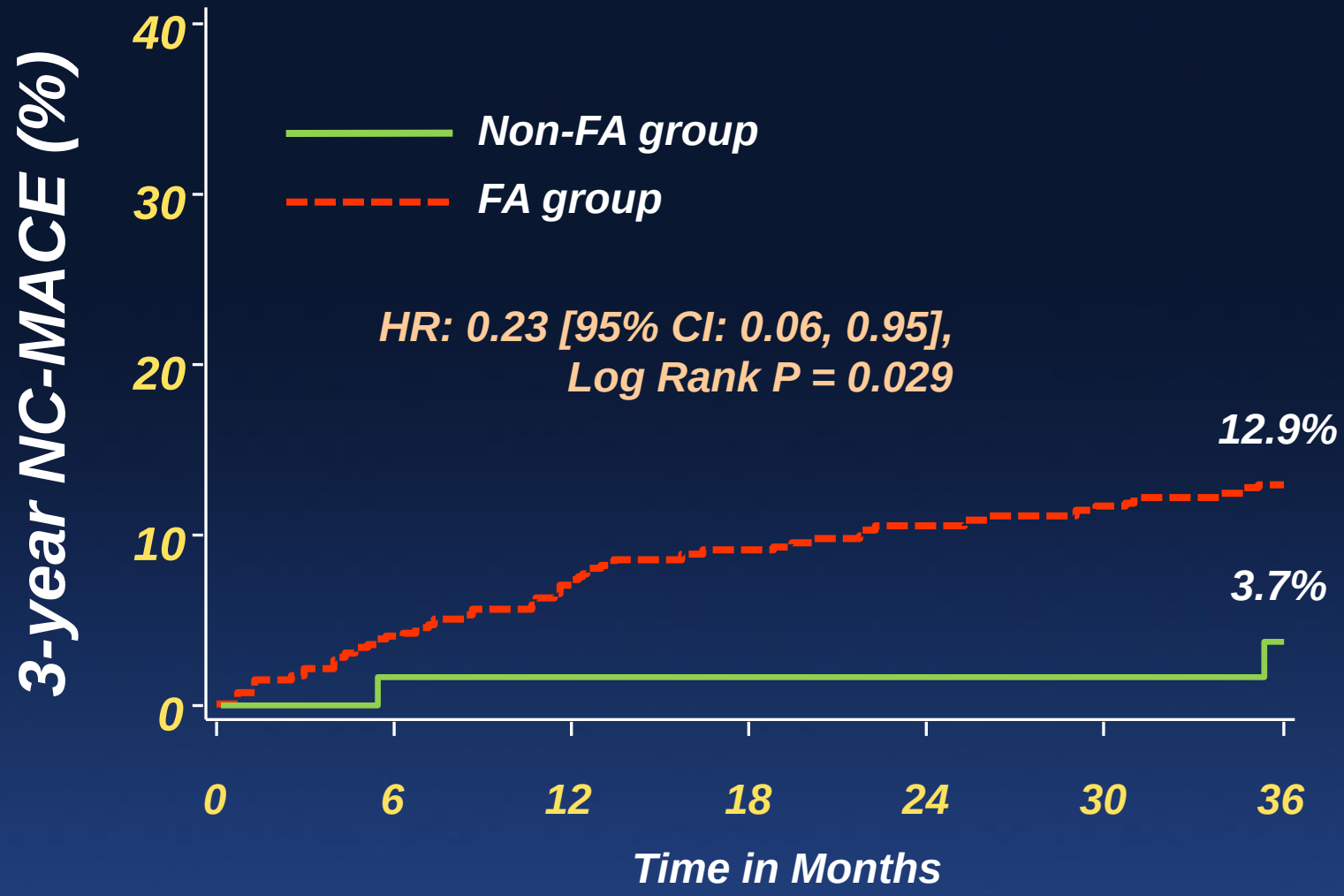
Stone et al. N Engl J Med 2011;361:226-35



Number at risk

Non-FA group	67	62	61	61	60	57	29
FA group	542	485	463	443	424	406	248

VIVA: Virtual Histology in Vulnerable Atherosclerosis

- *932 non-culprit lesions in 170 pts were identified with 3-vessel IVUS imaging*
- *At a median follow-up of 625 days, there were 18 culprit and non-culprit MACE in 16 pts*
- *14 revascularizations, 2 MIs, and 2 deaths*
- *Univariate predictors of non-culprit MACE*
- *Non-calcified VH-TCFA (p=0.025)*
- *MLA <4mm^2 (p=0.021)*
- *Plaque burden >70% (p<0.001)*
- *Remodeling index (p=0.014)*

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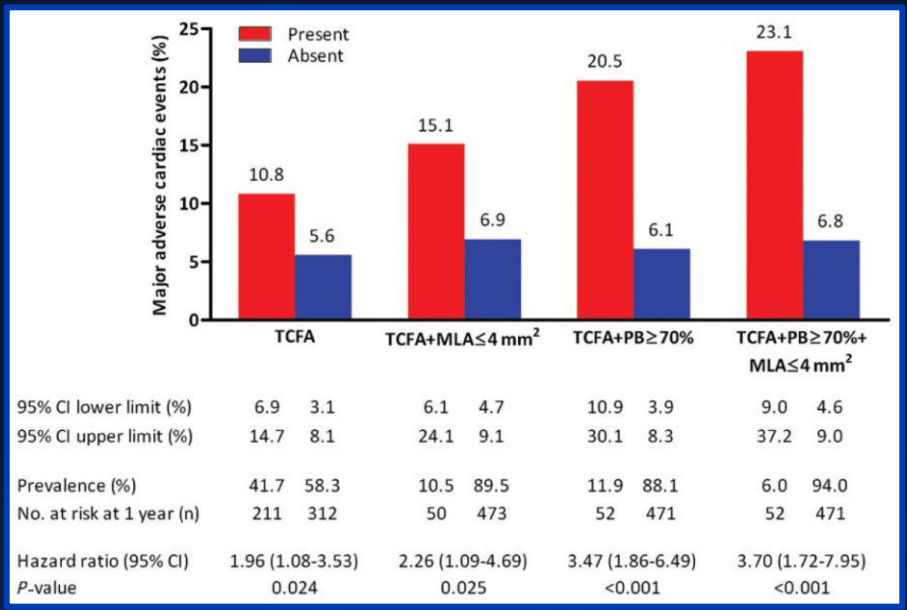
Calvert et al. JACC Cardiovasc Imaging 2011;4:894-901

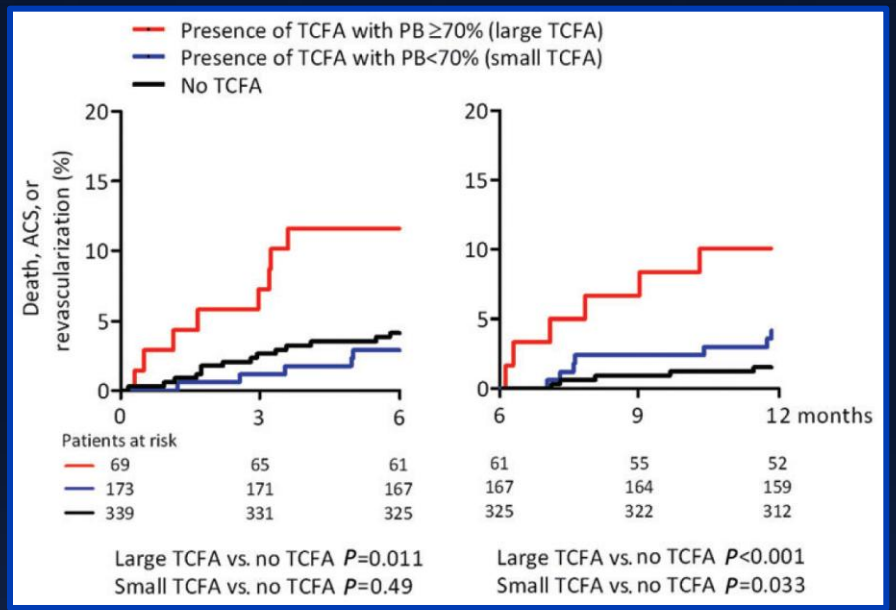
European Collaborative Project on Inflammation and Vascular Wall Remodeling in Atherosclerosis – Intravascular Ultrasound (ATHEROREMO-IVUS) study

- *1 non-culprit artery imaged in 581 pts (stable CAD or ACS): LAD>RCA>LCX*
- *At 1 year of follow-up, 56 pts had at least 1 event: 4 PCI in pts without baseline PCI, 11 culprit events, 27 non-culprit events, 18 indeterminate events*
- *18 deaths, 8 from cardiac or unknown causes; 14 ACS (7 MI); 24 unplanned revascularization*
- *Presence of VH-TCFA was significantly associated with the composite of Death/ACS (adjusted HR=2.51, p=0.021)*

Cheng et al. Eur Heart J, in press



	TCFA		TCFA+MLA≤4 mm²		TCFA+PB≥70%		TCFA+PB≥70%+ MLA≤4 mm²	
95% CI lower limit (%)	6.9	3.1	6.1	4.7	10.9	3.9	9.0	4.6
95% CI upper limit (%)	14.7	8.1	24.1	9.1	30.1	8.3	37.2	9.0
Prevalence (%)	41.7	58.3	10.5	89.5	11.9	88.1	6.0	94.0
No. at risk at 1 year (n)	211	312	50	473	52	471	52	471
Hazard ratio (95% CI)	1.96 (1.08-3.53)		2.26 (1.09-4.69)		3.47 (1.86-6.49)		3.70 (1.72-7.95)	
P-value	0.024		0.025		<0.001		<0.001	



- ***A VH-TCFA (present 10.8% vs. absent 5.6%; adjusted HR: 1.98, P=0.026) and a plaque burden ≥70% (present 16.2% vs. absent 5.5%; adjusted HR: 2.90, P<0.001), but not the presence of lesions with an MLA ≤4.0mm², were independently associated with MACE.***
- ***Risk for MACE was further increased if the VH-TCFA lesions had a MLA ≤4.0mm², plaque burden ≥70%, or a combination of these three characteristics***
- ***VH-TCFAs with a plaque burden ≥70% were associated with a higher MACE rate both in the first 6 months (P=0.011) and after 6 months (P<0.001), while smaller TCFA lesions were only associated with a higher MACE rate after 6 months (P=0.033)***
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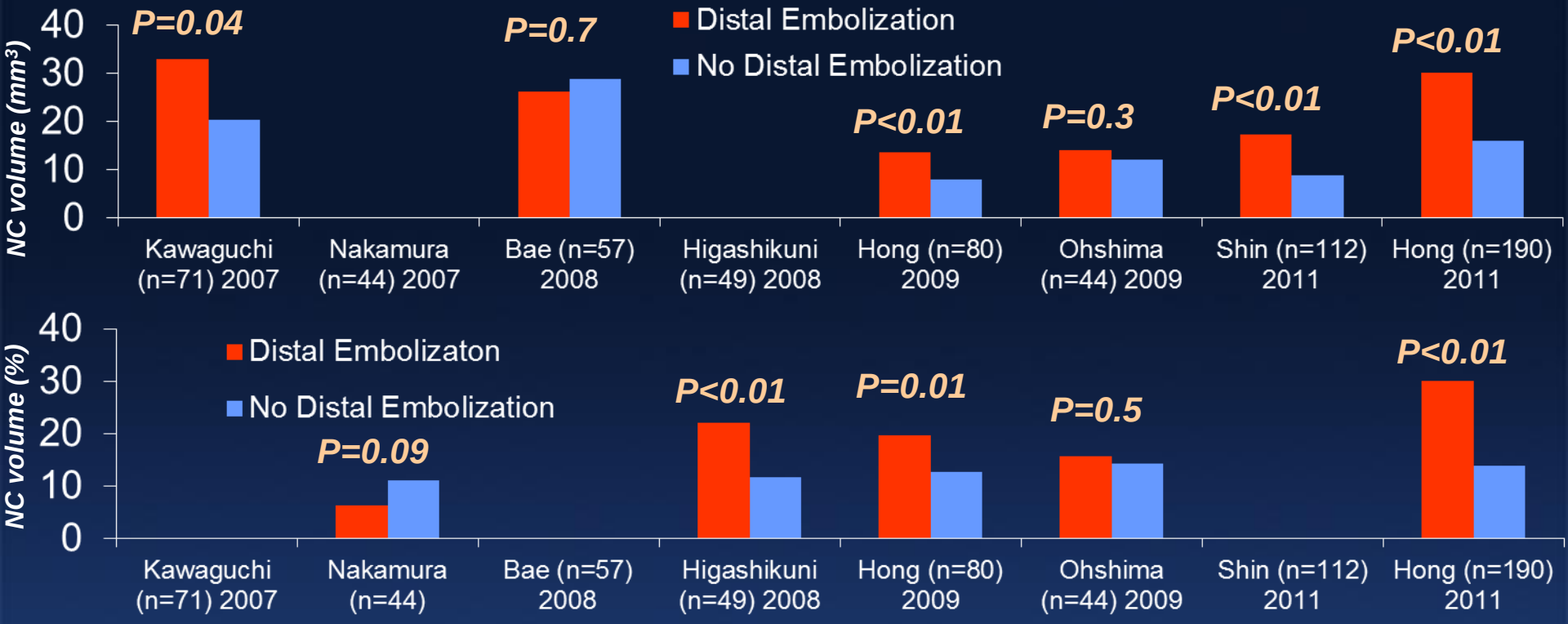
Cheng et al. Eur Heart J, in press

VH-IVUS and Peri-procedural MI



- *Kawamoto (n=44) 2007: NC an independent predictor of the tertile with the greatest # of HITS*
- *Bose (n=55) 2008: Strong correlations between NC and maximum increase in cardiac biomarkers*
- *Yamada (n=30) 2010: IMR improved post-PCI in the non-VH-TCFA group, but worsened in the VH-TCFA group*
- *Hong (n=190) 2011: ≥1 VH-TCFA or multiple VH-TCFAs more common in no-reflow*

Claessen et al. JACC Cardiovasc Imaging 2012;5:S111-8

A note of caution. . .
These and other VH-IVUS data do not apply to the two "competing" RF-IVUS technologies – IB-IVUS and iMAP

Conclusion

Despite its theroretical and practical limitations . . . in 3 prospective, core-lab and event-adjudication controlled studies in 1451 pts, VH-IVUS has been shown to identify TCFAs and predict adverse events